



PATENT

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re application of: Peter David DAVIS  
Serial No.: 09/890,989 Group No.: 1614  
Filed: December 14, 2001 Examiner.: Misook Yu  
For: COMBINATION FOR THE TREATMENT OF DISEASES INVOLVING  
ANGIOGENESIS

Attorney Docket No.: U 013589-7

Commissioner for Patents  
P.O. Box 1450  
Alexandria, VA 22313-1450

INFORMATION DISCLOSURE STATEMENT

Applicant calls the Examiner's attention to the documents annexed hereto as Annexes A, B and C, and listed on attached PTO Form 1449. Copies of the documents are also annexed.

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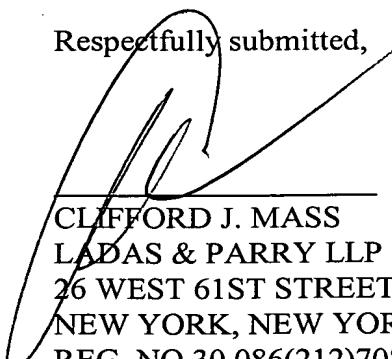
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Annex A, Tozer et al, was published after the priority date of the present application and contains data showing the potentiating effect of combining Combretastatin A4 with a number of NOS inhibitors including L-NNA and L-NAME (see Annex A figure 6 and p 1630 col. 1).

Annex B, Davis et al, further illustrates that a wide range of NOS inhibitors are effective when used in combination with Combretastatin A4. See in particular figure 1 on page 1533 of Annex B.

Annex C contains data that has been submitted for publication by Wachsberger et al. In Annex C it is shown that the co-administration of the vascular tubulin binding agent ZD6126 and the NOS inhibitor L-NNA was able to overcome resistance to ZD6126 in U87 glioblastoma cells (see Annex C, page 10 last paragraph to page 11, first paragraph, page 15 last paragraph and table 1). In particular Table 1 in Annex C clearly illustrates the enhanced tumour necrosis in this model obtained by dosing ZD6126 together with L-NNA.

Respectfully submitted,



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FORM PTO-1449		U. S DEPARTMENT OF COMMERCE PATENT AND TRADEMARK OFFICE		ATTY. DOCKET NO.	SERIAL NO.
				<b>U 013589-7</b>	<b>09/890,989</b>
				APPLICANT	
				<b>Peter David DAVIS</b>	
				FILING DATE	GROUP
				<b>December 14,</b>	<b>1614</b>
U. S. PATENT DOCUMENTS					
EXAMINER INITIALS	REFERENCE DESIGNATION	DOCUMENT NUMBER	DATE	NAME	FILING DATE IF APPROPRIATE
	AA				
	AB				
	AC				
	AD				
	AE				
	AF				
	AG				
	AH				
	AI				
	AJ				
	AK				
FOREIGN PATENT DOCUMENTS					
		DOCUMENT NUMBER	DATE	COUNTRY	TRANSLATION
					YES
	AL				
	AM				
	AN				
	AO				
	AP				
OTHER ART (Including Author, Title, Date, Pertinent Dates, Etc.)					
	AR	Annex A - Combretastatin A-4 Phosphate as a Tumor Vascular-Targeting Agent: Early Effects in Tumors and Normal Tissues: Tozer, Prise, Wilson, Locke, Vojnovic, Stratford, Dennis, Chaplin: Cancer Research 59, 1626-1634, April 1, 1999			
	AS	Annex B - Enhancement of Vascular Targeting by Inhibitors of Nitric Oxide Synthase: Davis, Tozer, Naylor, Thomson, Lewis, Hill: Int. J. Radiation Oncology Biol. Phys. Vol. 54, No. 5 pp. 1532-1536, 2002			
	AT	Annex C - Effect of the tumor vascular damaging agent, ZD6126 on the radioresponse of U97 glioblastoma: Wachsberger, Burd, Marrero, Daskalakis, Ryan, McCue, Dicker:			
EXAMINER			DATE CONSIDERED		
EXAMINER: Initial if citation considered, whether or not citation is in conformance with MPEP 609; Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.					